

### REMARKS

Claims 1-143 are pending. Claims 1-16, 65-134, 138, 139 and 141 are under examination. Claims 2-5, 33-57, 66-69, 91-94, and 105-134 have been canceled. Claims 65 and 81 have been amended. New claims 144-153 have been added. Support for the amendment and new claims can be found throughout the specification and the claims as filed. In particular, support for the amendment to claims 65 and 81 can be found, for example, on page 114, line 20, to page 115, line 3. Support for new claims 144-153 can be found, for example, in original claims 90 and 95-104. Accordingly, these amendments do not raise an issue of new matter, and entry thereof is respectfully requested.

Applicants appreciate the Examiner's reconsideration of the restriction requirement and rejoining of Groups I and IV.

### Rejections Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 1-16, 65-134, 138, 139 and 141 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement is respectfully traversed. Applicants respectfully submit that the specification provides sufficient description and guidance to enable the claimed methods.

The specification teaches a variety of methods for practicing the invention as claimed. In particular, the specification teaches that the methods of the invention can be used to diagnose the health state or disease state of an individual (page 11, lines 16-29). The specification also teaches statistical methods for determining the health state of an individual (page 12, line 19, to page 13, line 13; page 19, line 29, to page 21, line 29; page 23, line 13, to page 25, line 17; and page 39, line 22, to page 44, line 26). The specification additionally teaches methods for selecting a reference population and a sample of molecules predictive of the health state of an individual (page 70, line 1, to page 79, line 6). The specification further teaches that it is not necessary to determine the identity of the molecules for which the expression levels are determined (page 44, line 27, to page 45, line 7). Therefore, it is not necessary to determine what particular genes are associated with a disease state, in contrast to the

assertion in the Office Action regarding Cole et al., Nature Genet. 21:38-41 (1999), Risch, Nature 405:847-856 (2000), Lockhart and Winzeler, Nature 405:827-836 (2000), Roses, Nature 405:857-865 (2000).

Applicants respectfully submit that the specification provides sufficient description and guidance to enable the claimed methods. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

The rejection of claims 1-16, 65-134, 138, 139 and 141 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed. Applicants respectfully submit that the claims are clear and definite.

With regard to the terms “determining” and “comparing” as recited in independent claims 1, 65, 81, 90, 105, 138 and 141, Applicants respectfully submit that these terms are clear and definite. The specification teaches methods for determining and comparing expression levels and a multidimensional coordinate point, for example, on page 12, line 19, to page 13, line 13; page 19, line 29, to page 21, line 29; page 23, line 13, to page 25, line 17; and page 39, line 22, to page 44, line 26. Therefore, based on the teachings in the specification and what was well known to those skilled in the art for the meaning of these terms, Applicants maintain that these terms are clear and definite.

In regard to the indefiniteness rejection of claims 2, 3, 5, 66, 67, 69, 91, 92, 94, 106, 124, 125 and 127, Applicants maintain that these claims are clear and definite. Nevertheless, the rejection of these claims has been rendered moot by the cancellation of these claims.

In the Office Action, claims 65 and 81 are alleged to be indefinite in that the method does not meet the goal of the preamble. Claims 65 and 81 have been amended to recite “diagnosing a health state” to provide antecedent basis for the goal of the preamble.

Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

Rejections Under 35 U.S.C. § 102

The rejection of claims 1-16, 65-134, 138, 139 and 141 under 35 U.S.C. § 102(e) as allegedly anticipated by Friend et al., U.S. Patent No. 6,324,479, is respectfully traversed. Applicants respectfully submit that the claims are novel over Friend et al., '479.

Friend et al., '479, describes methods of determining protein activity levels using gene expression profiles. However, Friend et al., '479, does not teach the claimed methods of determining a comparative expression profile using a multidimensional coordinate point representative of expression levels of a sample of molecules in a population of molecules in a specimen from the individual or the claimed methods of determining a health state in an individual. Furthermore, Friend et al., '479, does not teach the claimed methods using a leukocyte specimen. Absent such a teaching, Friend et al., '479, cannot anticipate the claims. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 1-16, 65-134, 138, 139 and 141 under 35 U.S.C. § 102(e) as allegedly anticipated by Friend et al., U.S. patent application publication 2001/0018182, is respectfully traversed. Applicants respectfully submit that the claims are novel over Friend et al., '182.

Friend et al., '182, describes methods of monitoring disease states and therapies using gene expression profiles. However, Friend et al., '182, does not teach the claimed methods of determining a comparative expression profile using a multidimensional coordinate point representative of expression levels of a sample of molecules in a population of molecules in a specimen from the individual or the claimed methods of determining a health state in an individual. Furthermore, Friend et al., '182, does not teach the claimed methods using a leukocyte specimen. Absent such a teaching, Friend et al., '182, cannot anticipate the claims. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Inventors: Hood and Siegel  
Serial No.: 09/724,898  
Filed: November 28, 2000  
Page 18

**CONCLUSION**

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

Respectfully submitted,

Date: January 5, 2004



Deborah L. Cadena

Registration No. 44,048

Telephone: (858) 535-9001

Facsimile: (858) 535-8949

McDERMOTT, WILL & EMERY  
4370 La Jolla Village Drive  
Suite 700  
San Diego, California 92122